

REVISED VERSION

03 MAR 2005

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
18 March 2004 (18.03.2004)

PCT

(10) International Publication Number
WO 2004/022775 A1

(51) International Patent Classification⁷: **C12Q 1/18**,
C12N 15/74, C07C 235/64, 243/38, A61K 31/167, 31/15
// (C12Q 1/18, C12R 1:01) (C12N 15/74, C12R 1:01)

(74) Agent: CONIMAR AB; Box 2086, S-141 02 Huddinge
(SE).

(21) International Application Number:
PCT/SE2003/001381

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VC, VN, YU, ZA, ZM, ZW.

(22) International Filing Date:
4 September 2003 (04.09.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0202613-6 4 September 2002 (04.09.2002) SE

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): INNATE
PHARMACEUTICALS AB [SE/SE]; Umestan, S-903 47
Umeå (SE).

Published:
— with international search report

(72) Inventors; and
(75) Inventors/Applicants (*for US only*): KAUPPI, Anna,
Maria [SE/SE]; Morkullevägen 18M, S-906 51 Umeå
(SE). ELOFSSON, Jan, Mikael, Christian [SE/SE];
Sjöfruvägen 13, S-907 51 Umeå (SE). WOLF-WATZ,
Hans, Olof [SE/SE]; Djäkneböle 725, S-905 87 Umeå
(SE). NORDFELTH, Olov, Roland [SE/SE]; Bofinksvä-
gen 4B, S-906 51 Umeå (SE). DAHLGREN, Markus,
Kristoffer [SE/SE]; Birgittagatan 15B, S-414 53 Göteborg
(SE).

(88) Date of publication of the revised international search
report: 27 May 2004

(15) Information about Correction:
see PCT Gazette No. 22/2004 of 27 May 2004, Section II

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: METHODE ET SONDE D'IDENTIFICATION D'AGENTS MODIFICATEURS DE LA VIRULENCE BACTERI-
ENNE, AGENTS AINSI IDENTIFIES ET LEUR UTILISATION

(57) Abstract: L'invention porte sur un procédé d'identification d'agents antibactériens modificateurs de virulence comportant les étapes suivantes: épuiser en Ca₂₊ les bactéries d'une souche comprenant le gène hybride luxAB; incuber les bactéries épuisées en Ca₂₊ avec un agent dont l'effet antibactérien doit être déterminé; et enregistrer la lumière émise par les bactéries après adjonction d'un aldéhyde. L'incubation se fait à une température dépassant d'au moins 10 °C celle à laquelle les bactéries émettent de la lumière. L'invention porte également sur les sondes et sur les agents antibactériens identifiés au moyen dudit procédé.

WO 2004/022775 A1

REVISED
VERSION

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 2003/001381

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: C12Q 1/18, C12N 15/74, C07C 235/64, C07C 243/38, A61K 31/167, A61K 31/15
// (C12Q 1/18, C12R 1:01), (C12N 15/74, C12R 1:01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: C12Q, C12N, G01N, C07C, A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI-DATA, EPO-INTERNAL, PAJ, BIOSIS, MEDLINE, CHEM. ABS DATA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6136542 A (BRIGITTE DEMERS ET AL), 24 October 2000 (24.10.2000), see specially claims	1-12,22-23
A	--	13-21,24-29
Y	National Library of Medicine (NLM), file Medline, PMID: 8173809, Forsberg A: "In vivo expression of virulence genes of Yersinia pseudotuberculosis"; & Infect Agents Dis 1993 Aug;2(4):275-8	1-12,22-23
X	--	13-15
A	--	16-21,24-29

☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent but published on or after the international filing date	"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 19 February 2004	Date of mailing of the international search report 26-02-2004
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Micael Oswald/BS Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 03/01381

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ASM Abstract Database 2002 General Meeting (5/19/2002) through 5/23/2002) American Society for Microbiology, Vladimir Motin et al: "Genome-Wide Expression Profiling of Yersinia pestis During Low-Calcium Response", retrieved on 2003-04-04, http://www.asmtusa.org/memonly/abstracts/AbstractView.asp?AbstractID=62023	1-12,22-23
A	--	13-21,24-29
X	Infection and Immunity, Vol. 43, no. 1, January 1984, Ingrid Bölin et al: "Molecular Cloning of the Temperature-Inducible Outer Membrane Protein 1 of Yersinia pseudotuberculosis", page 72 - page 78	13-15
X	Molecular Microbiology, Vol. 2, no. 2, 1988, I. Bölin et al: "The plasmid-encoded Yop2b protein of Yersinia pseudotuberculosis is a virulence determinant regulated by calcium and temperature at the level of transcription", page 237 - page 245	13-15
X	STN International, File CAPLUS, CAPLUS accession no. 1968:95469, Document no. 68:95469, Ciampa, Giuseppe et al: "N-Substituted salicylamides. I. Halogenated 2-hydroxy- and 2-acetoxybenzanilides with antibacterial and antifungal activity"; & Rendiconto dell'Accademia delle Scienze Fisiche e Matematiche, Naples (1966), 33(Dec.), 386-95	16-19,21, 24-29
X	STN International, File CAPLUS, CAPLUS accession no. 1978:94851, Document no. 88:94851, "Anthelmintic compositions based on benzimidazoles"; & FR,A,2336931, 19770729	16-19,21, 24-29

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 03/01381

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STN International, File CAPLUS, CAPLUS accession no. 1979:16910, Document no. 90:16910, Shilakadze, E. M. et al: "Antituberculosis activity of beta- and gamma-pyridinecarboxylic acid phenylhydrazones and their manganese(II) and manganese(III) complexes"; & Soobshcheniya Akademii Nauk Gruzinskoi SSR (1978), 91(1), 145-8, esp. compound RN=68639-26-9 --	16-20,24-29
X	STN International, File CAPLUS, CAPLUS accession no. 1992: 645585, Document no. 117:245585, Ivanovo Agricultural Institute: "Method for treatment of fascioliasis and monieziasis in sheep"; & SU,A1,1715357, 19920228 --	16-19,21,24-29
X	GB 2365426 A (PANTHERIX LTD), 20 February 2002 (20.02.02) --	16-19,21,24-29
X	WO 0243668 A2 (WELLESLEY COLLEGE), 6 June 2002 (06.06.02), the claims and examples --	16-20,24-29
X	STN International, File CAPLUS, CAPLUS accession no. 1977:189559, Document no. 86:189559, Chinoin Gyogyszer es Vegyeszeti Termekek Gyara Rt., Hung.: "Salicylanilides"; & BE,A1,839873, 19760716 --	16-19,21,24-29
X	STN International, File CAPLUS, CAPLUS accession no. 1985:487603, Document no. 103:87603, Patel, J. M. et al: "Studies on antitubercular and antibacterial agents: preparation of 1-(4-aminobenzoyl)-2-benzalhydrazine and 1-(4-(phenylthioureido)benzoyl)-2-substituted-benzalhydrazine"; & Journal of the Indian Chemical Society (1984), 61(8), 718-20 --	16-20,24-29

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 03/01381

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STN International, File CAPLUS, CAPLUS accession no. 2002:298309, Document no. 137:169451, Kumar, Vipin et al: Synthesis and biological activities of 2-aryl-3-substituted benzamido-1,3-thiazolidin-4-ones"; & Indian Journal of Heterocyclic Chemistry (2002), 11(13), 251-252 --	16-20,24-29
X	J. Med. Chem., Vol. 41, 1998, Mark J. Macielag et al: "Substituted Salicylanilides as Inhibitors of Two-Component Regulatory Systems in Bacteria", page 2939 - page 2945 -----	16-19,21,24-29

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE03/01381

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: **16-19 and 27-29**
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

see next sheet

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE03/01381

Present claims 16-19 and 27-29 relate to an extremely large number of possible compounds. In fact, the claim contains so many options that a lack of clarity and conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible.

Consequently, the search has been carried out for those parts of the application which appear to be clear and concise, namely the compounds according to claims 20-21, 24-26, and structurally closely related compounds.

However, the initial phase of the search of these compounds revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims is impossible. Consequently, the search has been restricted to:
compounds as described above, and mainly those with antibacterial effect.

INTERNATIONAL SEARCH REPORT

Information on patent family members

31/10/03

International application No.

PCT/SE 03/01381

Patent document cited in search report			Publication date	Patent family member(s)		Publication date
US	6136542	A	24/10/00	US WO	6070290 A 9958714 A	06/06/00 18/11/99
GB	2365426	A	20/02/02	GB	0018887 D	00/00/00
WO	0243668	A2	06/06/02	AU AU WO	1178802 A 4173902 A 0235356 A	06/05/02 11/06/02 02/05/02